

CLAIMS

1. A use of a first agent that attenuates Topoisomerase I (Topo I) activity and a second agent that inhibits Heat Shock Protein 90 (HSP90) activity in the manufacture of a medicament for contemporaneous or sequential administration in chemotherapy.
2. The use according to claim 1 wherein the first agent is a compound selected from:
 - (i) compounds that bind to Topo I and inhibit its activity;
 - (ii) compounds which prevent the transcription, translation or expression of Topo I;
 - (iii) compounds which inhibit release of Topo I from intracellular stores; and
 - (iv) compounds which increase the rate of degradation of Topo I.
3. The use according to claim 1 or 2 wherein the first agent is a cleavable-complex inhibitor.
4. The use according to claim 1 or 2 wherein the first agent is Camptothecin or a derivative or analogue thereof.
5. The use according to claim 1 or 2 wherein the first agent is Topotecan or a derivative or analogue thereof.
6. The use according to claim 1 or 2 wherein the first agent is Irinotecan or a derivative or analogue thereof.
7. The use according to claim 1 or 2 wherein the first agent is Camptostar (CPT-11) or a derivative or analogue thereof.
8. The use according to claim 1 or 2 wherein the first agent is Gemcitabine or a derivative or analogue thereof.

9. The use according to any preceding claim wherein the second agent is a compound selected from:
- (i) compounds that bind to HSP 90 and inhibit its activity;
 - (ii) compounds which prevent the transcription, translation or expression of HSP 90;
 - (iii) compounds which inhibit release of HSP 90 from intracellular stores; and
 - (iv) compounds which increase the rate of degradation of HSP 90.
10. The use according to claim 9 wherein the second agent is Geldanamycin or a derivative or analogue thereof.
11. The use according to claim 10 wherein the second agent is 17-Allylamino,17-demethoxygeldanamycin (17AAG) or CNF-101.
12. The use according to claim 9 wherein the second agent is Radicicol or a derivative or analogue thereof.
13. The use according to any preceding claim wherein the chemotherapy is for cancer treatment.
14. The use according to claim 13 for the treatment of solid tumours.
15. The use according to claim 14 for the treatment of bowel cancer, small cell and non-small cell lung cancer, head and neck cancer, breast cancer, bladder cancer or malignant melanoma.
16. The use according to claim 15 for the treatment of paediatric tumours.
17. The use according to claim 13 or 16 for the treatment of neuroblastoma, leukaemias and lymphomas.

18. The use according to any one of claims 1 - 12 wherein the chemotherapy is for:

- antibacterial treatments;
- antifungal treatments;
- antiparasitic treatments;
- the treatment of AIDS/HIV;
- the treatment of multiple sclerosis; or
- the killing and inhibition of proliferation of any organism.

19. The use according to any preceding claim wherein the chemotherapy is for prophylactic treatment.

20. A delivery system for use in a gene therapy technique, said delivery system comprising:

- (i) a first DNA molecule encoding for a protein which directly or indirectly attenuates Topoisomerase I activity; and
- (ii) a second DNA molecule encoding for a protein which directly or indirectly inhibits Heat Shock Protein 90 activity;

wherein said DNA molecules are capable of being transcribed to allow the expression of said proteins and thereby be effective for chemotherapy.

21. The use of a delivery system according to claim 20 for the manufacture of a medicament for use in chemotherapy.

22. The use according to claim 21 for the treatment of conditions defined by any one of claims 12 to 19.

23. A method of screening a first and a second compound, to test whether or not said compounds has efficacy for use in combination as a chemotherapy, comprising:

- (a) exposing said compounds to Topoisomerase I and evaluating whether or not said compounds bind thereto;

- (b) exposing said compounds to Heatshock Protein 90 and evaluating whether or not said compounds bind thereto; and
- (c) selecting a first and second compound, wherein at least one compound binds to Topoisomerase I and at least one compound binds to Heatshock Protein 90 for use in combination as a chemotherapy.

24. A method of screening a compound, to test whether or not said compound has efficacy for use in chemotherapy, comprising exposing said compound to Topoisomerase I and Heatshock Protein 90 to evaluate whether or not said compound prevents interaction between Topoisomerase I and Heatshock Protein 90.

25. The method according to claim 23 or 24 wherein the compound is screened using Topoisomerase I and Heatshock Protein 90 as binding partners in an interaction trap and evaluating whether or not said compound modulates binding.

26. The method according to claim 25 wherein the interaction trap is a yeast two-hybrid interaction trap.

27. The method according to claim 26 wherein yeast used in the interact trap are permeable to the tested compounds.

28. A method of screening a compound, to test whether or not said compound is carcinogenic, comprising exposing said compound to Topoisomerase I and Heatshock Protein 90 to evaluate whether or not said compound promotes interaction between Topoisomerase I and Heat Shock Protein 90.

29. An *in vitro* method for diagnosing whether or not a subject has, or is likely to develop cancer, comprising:

- (i) detecting the level of activity or expression levels of Heat Shock Protein 90 and Topoisomerase I from a sample of cells from said subject;
- and

(ii) comparing the level of activity or expression levels of Heat Shock Protein 90 and Topoisomerase I in said sample relative to activity expression levels of Heat Shock Protein 90 and Topoisomerase I from a non-cancerous sample.

30. An *in vitro* method for evaluating the suitability of chemotherapeutic treatment for administration to a subject, comprising:

- (i) detecting the level of activity or expression levels of Heat Shock Protein 90 and Topoisomerase I from a sample of cells from said subject; and
- (ii) comparing the level of activity or expression levels of Heat Shock Protein 90 and Topoisomerase I in said sample relative to activity expression levels of Heat Shock Protein 90 and Topoisomerase I from a non-cancerous sample.

31. An *in vitro* method for monitoring the effectiveness of a chemotherapy for treating a subject, comprising:

- (i) detecting the level of activity or expression levels of Heat Shock Protein 90 and Topoisomerase I from a sample of cells from said subject; and
- (ii) comparing the level of activity or expression levels of Heat Shock Protein 90 and Topoisomerase I in said sample relative to activity expression levels of Heat Shock Protein 90 and Topoisomerase I from a non-cancerous sample.